ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Datroway 100 mg powder for concentrate for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One vial of powder for concentrate for solution for infusion contains 100 mg of datopotamab deruxtecan. After reconstitution, one vial of 5 mL solution contains 20 mg/mL of datopotamab deruxtecan (see section 6.6).

Datopotamab deruxtecan is an antibody-drug conjugate (ADC) that contains a humanised anti-TROP2 IgG1 monoclonal antibody (mAb) produced by mammalian (Chinese Hamster Ovary) cells, covalently linked to DXd, an exatecan derivative and a topoisomerase I inhibitor, via a tetrapeptide-based cleavable linker. Approximately 4 molecules of deruxtecan are attached to each antibody molecule.

Excipient with known effect

Each 100 mg vial contains 1.50 mg of polysorbate 80 (E 433).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for concentrate for solution for infusion.

White to yellowish white lyophilised powder, which has a cake-like appearance.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Breast cancer

Datroway as monotherapy is indicated for the treatment of adult patients with unresectable or metastatic hormone receptor (HR)-positive, HER2-negative breast cancer who have received endocrine therapy and at least one line of chemotherapy in the advanced setting (see section 5.1).

4.2 Posology and method of administration

Datroway should be prescribed by a physician and administered under the supervision of a healthcare professional experienced in the use of anticancer medicinal products.

Patient selection

Patients for treatment of unresectable or metastatic HR-positive, HER2-negative breast cancer should be selected on the basis of a documented HER2-negative result assessed by a CE marked IVD if available, or an alternative validated test.

Posology

The recommended dose of Datroway is 6 mg/kg (up to a maximum of 540 mg for patients ≥90 kg) of body weight given as an intravenous infusion once every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity.

Premedication and prophylactic medicinal products

Prior to each infusion of Datroway, a premedication regimen for the prevention of infusion-related reactions that consists of an antihistamine and paracetamol (with or without glucocorticoids) should be considered (see section 4.8).

It is also recommended that patients receive prophylactic antiemetic agents (dexamethasone with 5-HT3 antagonists as well as other medicinal products, such as NK1 receptor antagonists) prior to infusion of Datroway and on subsequent days as needed.

For prophylactic treatment for keratitis and stomatitis, see section 4.4.

Dose modifications

Dose modifications for infusion-related reactions
The infusion rate of Datroway should be slowed or interrupted if the patient develops an infusion-related reaction. Datroway should be permanently discontinued in case of life-threatening infusion-related reactions.

Dose modifications for adverse reactions
Management of adverse reactions may require dose delay, dose reduction, or treatment discontinuation per guidelines provided in Tables 1 and 2.

Datroway dose should not be re-escalated after a dose reduction is made.

Table 1: Dose reductions for adverse reactions

Recommended starting dose	6 mg/kg (up to a maximum of 540 mg for patients ≥90 kg)
First dose reduction	4 mg/kg (up to a maximum of 360 mg for patients ≥90 kg)
Second dose reduction	3 mg/kg (up to a maximum of 270 mg for patients ≥90 kg)

Table 2: Dose modifications for adverse reactions

Adverse reaction	Severity*	Dose modification
Interstitial lung disease (ILD)/pneumonitis *[see sections 4.4 and 4.8]*	Asymptomatic ILD/pneumonitis (Grade 1)	Delay dose until resolved to Grade 0#, then: • if resolved in 28 days or less from date of onset, maintain dose. • if resolved in greater than 28 days from date of onset, reduce dose one level (see Table 1). • consider corticosteroid treatment as soon as ILD/pneumonitis is suspected.
	Symptomatic ILD/pneumonitis (Grade 2 or greater)	• Permanently discontinue. • Promptly initiate corticosteroid treatment as soon as ILD/pneumonitis is suspected.

Adverse reaction	Severity*	Dose modification
Keratitis *[see sections 4.4 and 4.8]*	Grade 2	• Delay dose until resolved to Grade 1 or less, then maintain dose.
	Grade 3	• Delay dose until resolved to Grade 1 or less, then reduce the dose by 1 level (see Table 1).
	Grade 4	• Permanently discontinue.
Stomatitis *[see sections 4.4 and 4.8]*	Grade 2	• Delay dose until resolved to Grade 1 or less. • Restart at the same dose for first occurrence. • Consider restarting at reduced dose level (see Table 1) if recurrent.
	Grade 3	• Delay dose until resolved to Grade 1 or less. • Restart at reduced dose level (see Table 1).
	Grade 4	• Permanently discontinue.

***** Per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 5.0.

[#] Grade 0 refers to full resolution of ILD/pneumonitis, including the disappearance of radiological findings associated with active ILD/pneumonitis. Residual scarring or fibrosis following recovery of ILD/pneumonitis is not considered to be active disease.

Delayed or missed dose

If a planned dose is delayed or missed, it should be administered as soon as possible without waiting until the next planned cycle. The schedule of administration should be adjusted to maintain a 3-week interval between doses.

Special populations

Elderly
No dose adjustment of Datroway is required in patients aged 65 years or older. Data from datopotamab deruxtecan in patients aged 85 years or older are limited.

Renal impairment
No dose adjustment is required in patients with mild to moderate (creatinine clearance [CLcr] ≥ 30 and < 90 mL/min) renal impairment (see section 5.2). The recommended dosage of Datroway has not been established in patients with severe renal impairment (see section 5.2). Patients with severe renal impairment should be monitored carefully. In patients with moderate renal impairment at baseline who received datopotamab deruxtecan 6 mg/kg, a higher incidence of serious adverse reactions was observed compared to those with normal renal function.

Hepatic impairment
No dose adjustment is required in patients with mild (total bilirubin ≤ upper limit of normal (ULN) and any aspartate aminotransferase (AST) > ULN or total bilirubin > 1 to 1.5 times ULN and any AST) hepatic impairment. There are limited data to make a recommendation on dose adjustment in patients with moderate (total bilirubin > 1.5 to 3 times ULN and any AST) hepatic impairment. Insufficient data are available in patients with severe (total bilirubin > 3 times ULN and any AST) hepatic impairment. Therefore, patients with moderate and severe hepatic impairment should be monitored carefully (see section 4.4 and 5.2).

Paediatric population
The safety and efficacy in children and adolescents below 18 years of age have not been established. No data are available.

Method of administration

Datroway is for intravenous use. It must be reconstituted and diluted by a healthcare professional and administered as an intravenous infusion. Datroway must not be administered as an intravenous push or bolus.

The first infusion is to be administered over 90 minutes. Patients should be observed during the infusion and for at least 30 minutes following the initial dose for signs or symptoms of infusion-related reactions.

Subsequent infusions are to be administered over 30 minutes if prior infusions were tolerated. Patients should be observed during the infusion and for at least 30 minutes after infusion.

Precautions to be taken before handling or administering the medicinal product

This medicinal product contains a cytotoxic component, which is covalently attached to the monoclonal antibody (see special handling and disposal procedures in section 6.6).

For instructions on reconstitution and dilution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Interstitial lung disease/pneumonitis

Cases of interstitial lung disease (ILD), including pneumonitis, have been reported in patients treated with Datroway (see section 4.8). Fatal outcomes have been observed.

Patients should be advised to immediately report cough, dyspnoea, fever, and/or any new or worsening respiratory symptoms. Patients should be monitored for signs and symptoms of ILD/pneumonitis. Evidence of ILD/pneumonitis should be promptly investigated. Patients with suspected ILD/pneumonitis should be evaluated by radiographic imaging. Consultation with a pulmonologist should be considered. For asymptomatic (Grade 1) ILD/pneumonitis, consider corticosteroid treatment (e.g. ≥ 0.5 mg/kg/day prednisolone or equivalent). Datroway should be delayed until recovery to Grade 0 and may be resumed according to instructions in Table 2 (see section 4.2). For symptomatic ILD/pneumonitis (Grade 2 or greater), promptly initiate systemic corticosteroid treatment (e.g. ≥ 1 mg/kg/day prednisolone or equivalent) and continue for at least 14 days followed by gradual taper for at least 4 weeks. Datroway should be permanently discontinued in patients who are diagnosed with symptomatic (Grade 2 or greater) ILD/pneumonitis (see section 4.2). Patients with a history of ILD/pneumonitis may be at increased risk of developing ILD/pneumonitis and should be monitored carefully.

Keratitis

Datroway can cause ocular surface undesirable effects including keratitis. Signs and symptoms of keratitis may include dry eye, increased lacrimation, photophobia, and detrimental changes to vision (see section 4.8).

Patients should be advised to use preservative-free lubricant eye drops several times daily for prophylaxis. Patients should be advised to avoid use of contact lenses unless directed by an eye care professional. Patients should be promptly referred for appropriate ophthalmologic assessments for any new or worsening ocular signs and symptoms that could suggest keratitis. Keratitis should be monitored and if diagnosis is confirmed, Datroway should be dose delayed, dose reduced, or permanently discontinued (see section 4.2).

Patients with clinically significant corneal disease were excluded from the study (see section 5.1). Patients with pre-existing keratitis should be carefully monitored.

Stomatitis

Stomatitis, including mouth ulcers and oral mucositis, have been reported in patients being treated with Datroway (see section 4.8).

In addition to practicing good oral hygiene, when starting Datroway and throughout treatment, daily use of a steroid-containing mouthwash (e.g. dexamethasone oral solution 0.1 mg/mL 4 times daily or a similar steroid-containing mouthwash regimen) is recommended for prophylaxis and treatment. Where clinically indicated, antifungal agents may be considered in accordance with local guidelines. In the absence of a prophylactic steroid-containing mouthwash, use of bland mouth rinses (e.g. a non-alcoholic and/or bicarbonate-containing mouthwash) per local guidelines is recommended. Ice chips or ice water held in the mouth throughout the infusion may also be considered. If stomatitis does occur, frequency of mouthwashes may be increased and/or other topical treatments may be used. Based on the severity of the adverse reaction, dose delay, dose reduce, or permanently discontinue Datroway (see section 4.2).

Embryo-foetal toxicity

Based on findings in animals and its mechanism of action, the topoisomerase I inhibitor component of Datroway can cause embryo-foetal harm when administered to a pregnant woman.

The pregnancy status of females of childbearing potential should be verified prior to the initiation of Datroway. The patient should be informed of the potential risks to the foetus. Females of reproductive potential should be advised to use effective contraception during treatment and for at least 7 months following the last dose of Datroway. Male patients with female partners of reproductive potential should be advised to use effective contraception during treatment with Datroway and for at least 4 months after the last dose of Datroway (see section 4.6).

Patients with moderate or severe hepatic impairment

There are limited data in patients with moderate hepatic impairment and severe hepatic impairment. As metabolism and biliary excretion are the primary routes of elimination of the topoisomerase I inhibitor, DXd, Datroway should be administered with caution in patients with moderate and severe hepatic impairment (see sections 4.2 and 5.2).

Excipient with known effect

This medicine contains 1.5 mg of polysorbate 80 in each vial. Polysorbates may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

No clinical drug interaction studies with datopotamab deruxtecan have been conducted. However, clinical drug-drug interaction studies were conducted with trastuzumab deruxtecan (T-DXd), which contains the same DXd payload as Datroway. The C_{max} of DXd was not affected by ritonavir (inhibitor of CYP3A4 and OATP1B1 and 1B3) or itraconazole (inhibitor of CYP3A4). The AUC was increased 1.2-fold by both inhibitors which was not considered clinically relevant. Therefore, inhibitors of CYP3A4, OATP1B1 and OATP1B3 will most likely not have a clinically relevant effect on the PK of deruxtecan released from datopotamab deruxtecan.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/Contraception in females and males

The pregnancy status of women of childbearing potential should be verified prior to initiation of Datroway.

Women of childbearing potential should use effective contraception during treatment with Datroway and for at least 7 months following the last dose.

Men with female partners of childbearing potential should use effective contraception during treatment with Datroway and for at least 4 months following the last dose.

Pregnancy

There are no available data on the use of Datroway in pregnant women. However, based on findings in animals and its mechanism of action, the topoisomerase I inhibitor component, DXd, can be expected to cause embryo-foetal harm when administered to pregnant women (see section 5.3).

Datroway is not recommended during pregnancy and in women of childbearing potential not using contraception. Patients should be informed of the potential risks to the foetus before they become pregnant and to contact their doctor immediately if they become pregnant.

Breast-feeding

It is not known if datopotamab deruxtecan is excreted in human milk. Human IgG is excreted in human milk. Because of the potential for serious adverse reactions in breast-fed children, women should discontinue breast-feeding prior to initiating treatment with Datroway. Women may begin breast-feeding 1 month after concluding treatment.

Fertility

No human data on the effect of datopotamab deruxtecan on fertility are available. Based on results from animal toxicity studies, Datroway may impair male and female reproductive function and fertility (see section 5.3).

Both men and women should seek advice on fertility preservation before treatment. It is not known whether datopotamab deruxtecan or its metabolites are found in seminal fluid. Male patients must not freeze or donate sperm throughout the treatment period, and for at least 4 months after the final dose of Datroway. Females must not donate, or retrieve for their own use, ova throughout the treatment period and for at least 7 months after the final dose of Datroway.

4.7 Effects on ability to drive and use machines

Datroway may influence the ability to drive and use machines. Patients should be advised to use caution when driving or operating machines in case they experience fatigue or vision changes during treatment with Datroway (see section 4.8).

4.8 Undesirable effects

Summary of safety profile

The pooled safety profile has been assessed from two clinical studies involving 443 patients who received Datroway 6 mg/kg body weight for the treatment of breast cancer. The median exposure to Datroway in this data set was 6.2 months (range 0.7 to 28.5 months).

The most common adverse reactions were stomatitis (64.8%), nausea (57.6%), fatigue (42.7%), alopecia (37.2%), constipation (33.0%), vomiting (26.0%), dry eye (25.5%), COVID-19 (17.8%), keratitis (17.8%), anaemia (17.2%), decreased appetite (16.3%), AST increased (16.0%), rash (15.3%), diarrhoea (12.9%), neutropenia (12.0%) and alanine aminotransferase (ALT) increased (10.4%).

The most common Grade 3/4 adverse reactions were stomatitis (7.9%), fatigue (4.3%), anaemia (3.2%), AST increased (2.7%), vomiting (1.6%), ALT increased (1.6%), nausea (1.4%), urinary tract infection (1.4%), COVID-19 (1.1%), decreased appetite (1.1%), neutropenia (1.1%) and pneumonia (1.1%). Grade 5 adverse reactions occurred in 0.7% of patients and were due to ILD/pneumonitis, dyspnoea and sepsis.

The most common serious adverse reactions were COVID-19 (1.4%), urinary tract infection (1.1%), ILD/pneumonitis (1.1%) and sepsis (1.1%).

The frequency of treatment discontinuation due to adverse reactions was 3.6%. The most common adverse reaction leading to treatment discontinuation was ILD/pneumonitis (2.0%). The frequency of dose reductions due to adverse reactions was 21.0%. The most common adverse reactions leading to dose reduction were stomatitis (12.9%), fatigue (3.2%), nausea (1.8%) and keratitis (1.4%). The frequency of dose interruptions due to adverse reactions was 19.6%. The most common adverse reactions leading to dose interruption were stomatitis (5.2%), COVID-19 (4.1%), fatigue (2.3%), ILD/pneumonitis (1.6%), pneumonia (1.6%), keratitis (1.4%) and infusion-related reaction (1.1%).

Tabulated list of adverse reactions

Table 3 presents adverse reactions reported with Datroway. Adverse reactions are listed by System Organ Class and frequency category. The adverse reaction frequencies are based on all-cause adverse event frequencies, where a proportion of the events for an adverse reaction may have other causes than datopotamab deruxtecan, such as the disease, other medicinal products or unrelated causes. The severity of adverse drug reactions was assessed based on the Common Terminology Criteria for Adverse Events (CTCAE), defining Grade 1 = mild, Grade 2 = moderate, Grade 3 = severe, Grade 4 = life threatening, and Grade 5 = death.

Frequency categories are defined as: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1 000 to < 1/100), rare (≥ 1/10 000 to < 1/1 000), very rare (< 1/10 000), and not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.

Table 3: Adverse reactions in patients treated with datopotamab deruxtecan 6 mg/kg

System organ class	Frequency category	Adverse reactions
Infections and infestations		
	Very common	COVID-19[a]
	Common	urinary tract infection, pneumonia[b], sepsis
Blood and lymphatic system disorders		
	Very common	anaemia, neutropenia[c]
	Common	leukopenia

System organ class	Frequency category	Adverse reactions
Metabolism and nutrition disorders		
	Very common	decreased appetite
Nervous system disorders		
	Common	dysgeusia
Eye disorders		
	Very common	keratitis[d], dry eye
	Common	conjunctivitis[e], blurred vision, lacrimation increased, blepharitis, meibomian gland dysfunction, photophobia
	Uncommon	visual impairment
Respiratory, thoracic and mediastinal disorders		
	Common	ILD/pneumonitis[f], dyspnoea
Gastrointestinal disorders		
	Very common	stomatitis[g], vomiting, nausea, diarrhoea, constipation
	Common	dry mouth
Skin and subcutaneous tissue disorders		
	Very common	alopecia, rash[h]
	Common	pruritus, dry skin, skin hyperpigmentation[i], madarosis
General disorders and administration site conditions		
	Very common	fatigue[j]
Investigations		
	Very common	aspartate aminotransferase increased, alanine aminotransferase increased
Injury, poisoning and procedural complications		
	Common	infusion-related reaction[k]

[a] Including COVID-19, COVID-19 pneumonia, SARS-CoV-2 test positive.
[b] Including pneumonia, lower respiratory tract infection and lower respiratory tract infection fungal.
[c] Including neutropenia and neutrophil count decreased.
[d] Including keratitis, punctate keratitis and ulcerative keratitis.
[e] Including conjunctivitis, conjunctival disorder, conjunctival hyperaemia and conjunctival irritation.
[f] Including interstitial lung disease and pneumonitis.
[g] Including stomatitis, aphthous ulcer, glossitis, mouth ulceration, odynophagia, oral pain, oropharyngeal pain and pharyngeal inflammation.
[h] Including rash, erythematous rash, maculo-papular rash and pruritic rash.
[i] Including skin hyperpigmentation and skin discolouration.
[j] Including fatigue and asthenia.
[k] Infusion-related reaction includes as any reaction (infusion-related reaction, pruritus and rash) occurring within the same day as Datroway infusion.

Description of selected adverse reactions

Interstitial lung disease/pneumonitis

ILD/pneumonitis occurred in 4.7% of the pool of patients with breast cancer treated with Datroway 6 mg/kg, of which 3.6% were adjudicated as drug-related ILD/pneumonitis by independent review. Most ILD/pneumonitis cases were Grade 1 (2.9%). Grade 2 events occurred in 0.9% of patients. Grade 3 events occurred in 0.9% of patients. Adjudicated drug-related Grade 5 events occurred in 0.2% of patients. Median time to first onset was 5.8 months (range: 1.1 to 10.8).

Ocular surface undesirable effects

Ocular surface undesirable effects occurred in 49.0% of the pool of patients treated with Datroway, of which 35.0% were Grade 1, 12.2% were Grade 2 and 1.8% were Grade 3. Keratitis occurred in 17.8% of the pool of patients treated with Datroway, of which 13.3% were Grade 1, 3.6% were Grade 2 and 0.9% were Grade 3. The median time to onset was 4.1 months (range: 0 to 23.2). Discontinuation due to keratitis occurred in 0.5% of patients.

Stomatitis

Stomatitis occurred in 64.8% of the pool of patients treated with Datroway, of which 29.3% were Grade 1, 27.5% were Grade 2 and 7.9% were Grade 3. Median time to first onset was 0.6 months (range: 0.03 to 12.2). Discontinuation due to stomatitis occurred in 0.5% of patients.

Haematological events

In study TROPION-Breast01 neutropenia occurred in 11.7% of patients treated with Datroway (1.1% were Grade ≥3). Leukopenia occurred in 3.6% of patients treated with Datroway (none were Grade ≥3). Colony stimulating factor was used by 2.7% of patients treated with Datroway.

Elderly

Of the 443 patients with breast cancer treated with Datroway 6 mg/kg, 23.3% were 65 years or older and 4.7% were 75 years or older. Data are limited to establish the safety in patients 85 years or older.

There was a numerically lower proportion of Grade 3/4 adverse reactions (24.3% vs 25.0%) and a numerically higher proportion of serious adverse reactions (9.7% vs 6.8%) and adverse reactions leading to discontinuation (3.9% vs 3.5%) observed in patients aged 65 years or older compared to patients younger than 65 years old.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

There is currently no specific treatment in the event of an overdose. Higher than the indicated dosing may increase risk of adverse reactions. Physicians should follow general supportive measures and institute appropriate treatment.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antineoplastic agents, monoclonal antibodies and antibody drug conjugates, ATC code: L01FX35

Mechanism of action

Datopotamab deruxtecan is a TROP2-directed antibody-drug conjugate. The antibody is a humanised anti-TROP2 IgG1 attached to deruxtecan, a topoisomerase I inhibitor (DXd) bound by a tetrapeptide-based cleavable linker. The antibody-drug conjugate is stable in plasma. The antibody binds to TROP2 expressed on the surface of certain tumour cells. After binding, datopotamab

deruxtecan undergoes internalisation into the tumour cells. Subsequently, the release of DXd results in DNA damage and apoptotic cell death via topoisomerase I inhibition. Datopotamab deruxtecan may also exhibit indirect cytotoxicity as shown in vitro through mechanisms of antibody-dependent cellular cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP) and bystander cytotoxicity of DXd against TROP2 expressing tumour cells and neighbouring cells.

Pharmacodynamic effects

Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity.
During the median 5.5 month treatment period across clinical studies in NSCLC and breast cancer patients treated with Datroway at 6 mg/kg, the incidence of anti-datopotamab deruxtecan antibodies was 16% (146 out of 912) and the incidence of neutralising antibodies against datopotamab deruxtecan was 2.5% (23 out of 912). There was no apparent effect of anti-drug antibodies on the pharmacokinetics or effectiveness of datopotamab deruxtecan. No clinically meaningful impact on the safety of datopotamab deruxtecan was observed.

Clinical efficacy and safety

HR+/HER2- breast cancer

TROPION-Breast01 (NCT05104866)
The efficacy of Datroway was evaluated in study TROPION-Breast01, a multicentre, open-label, randomised study of 732 patients with unresectable or metastatic HR-positive, HER2-negative (IHC 0, IHC1+ or IHC2+/ISH-) breast cancer. Patients must have progressed on and been unsuitable for endocrine therapy. Patients were required to have received 1 to 2 lines of prior chemotherapy in the unresectable or metastatic disease setting. Patients with clinically inactive brain metastases were included in the study. Patients were excluded for a history of ILD/pneumonitis requiring treatment with steroids, ongoing ILD/pneumonitis, or clinically significant cardiac, pulmonary or corneal disease at screening. Patients were also excluded for Eastern Cooperative Oncology Group (ECOG) performance status > 1.

A total of 732 patients were randomised 1:1 to receive either Datroway 6 mg/kg (N=365) by intravenous infusion every 3 weeks or physician's choice of chemotherapy (N=367, eribulin 59.9%, capecitabine 20.7%, vinorelbine 10.4% or gemcitabine 9.0%) until unacceptable toxicity or disease progression. Randomisation was stratified by previous lines of chemotherapy (one or two), prior treatment with a CDK4/6 inhibitor (yes or no) and geographical region (United States, Canada, Europe, or Rest of World). Tumour imaging was obtained every 6 weeks until disease progression.

The dual primary efficacy endpoints were progression-free survival (PFS) as assessed by blinded independent central review (BICR) based on Response Evaluation Criteria in Solid Tumours (RECIST) v.1.1 and overall survival (OS). Confirmed objective response rate (ORR) and duration of response (DOR) were secondary endpoints.

Baseline demographics and disease characteristics were similar between treatment arms. The median age was 55 years (range 28 to 86); 22.3% were ≥ 65 years and 98.8% were female; 47.8% were White, 1.5% were Black or African American, 40.7% were Asian and 11.3% were of Hispanic/Latino ethnicity; 57% had ECOG PS 0 and 42.3% had ECOG PS of 1; 97.3% had visceral disease, 71.9% had liver metastases and 7.9% had stable brain metastases at baseline at the time of randomisation.

There were 60.2% of patients who received prior endocrine therapy in the (neo) adjuvant setting, 88.5% received prior endocrine therapy in the unresectable or metastatic setting and all patients received prior chemotherapy regimens in the unresectable or metastatic setting. Overall, 80.7% of patients had received prior taxanes and 63.8% had received prior anthracyclines. There were 62% of patients who had 1 prior chemotherapy regimen and 37.7% of patients who had 2 prior chemotherapy

regimens for treatment of unresectable or metastatic disease. 82.5% of patients had prior treatment with a CDK4/6 inhibitor.

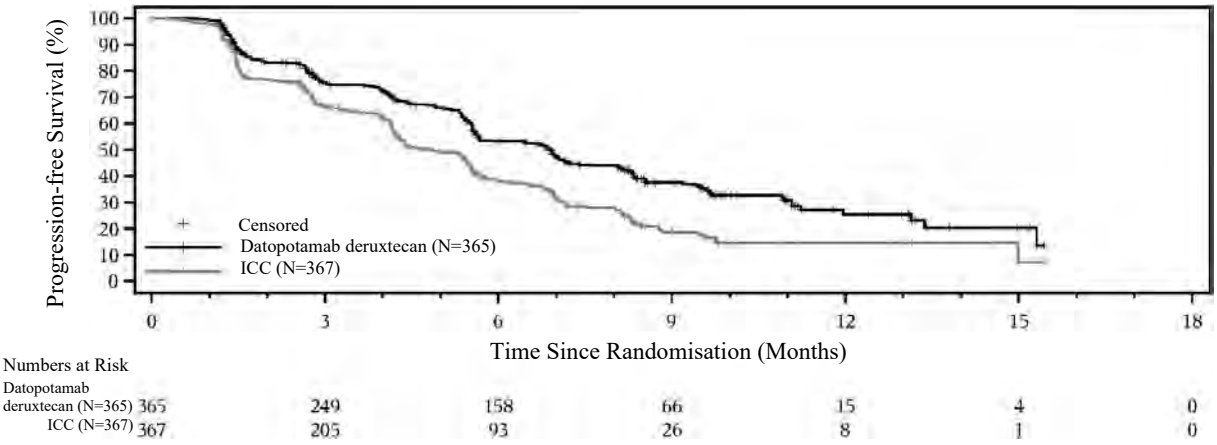
Efficacy results are shown in Table 4 and Figure 1 and 2.

Table 4: Efficacy results in TROPION-Breast01

Efficacy parameter	**Datroway (N=365)**	**Chemotherapy (N=367)**
Progression-free survival by BICR[a]		
Number of events (%)	212 (58.1)	235 (64.0)
Median, months (95% CI)	6.9 (5.7, 7.4)	4.9 (4.2, 5.5)
Hazard ratio (95% CI)	0.63 (0.52, 0.76)	
p-value[b]	< 0.0001	
Overall Survival[c, d]		
Number of events (%)	223 (61.1)	213 (58.0)
Median, months (95% CI)	18.6 (17.3, 20.1)	18.3 (17.3, 20.5)
Hazard ratio (95% CI)	1.01 (0.83, 1.22)	
p-value[e]	0.9445	
Objective response rate by BICR[a, f]		
n (%)	133 (36.4)	84 (22.9)
95% CI	31.4, 41.3	18.6, 27.2
Duration of response by BICR[a, f]		
Median, months (95% CI)	6.7 (5.6, 9.8)	5.7 (4.9, 6.8)

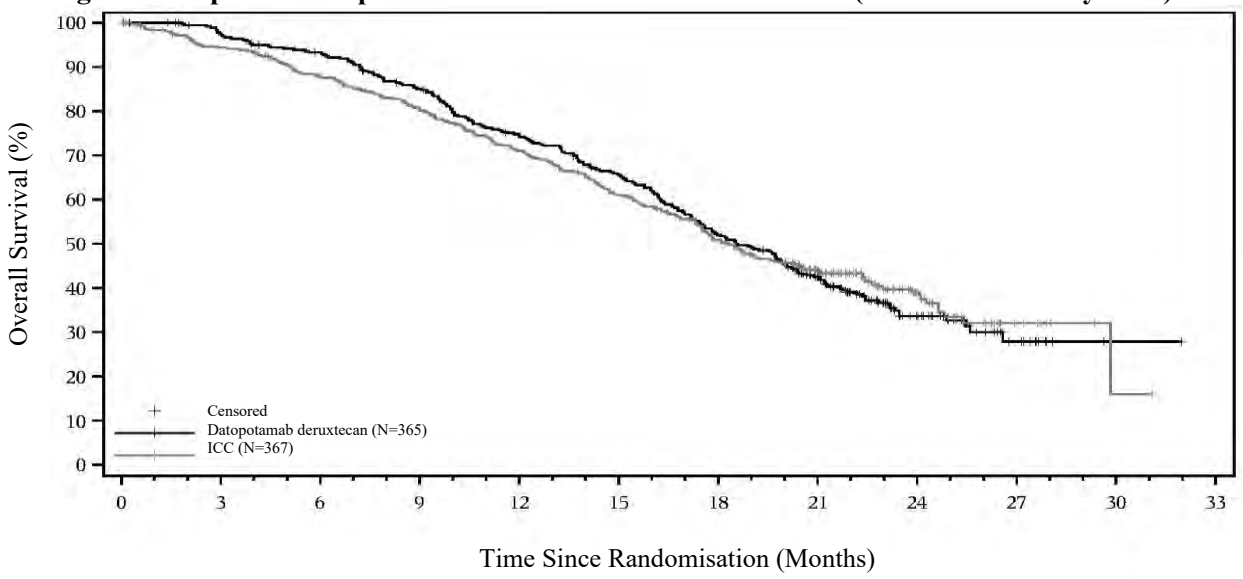
[a] Data cutoff 17 July 2023
[b] Predefined p-value boundary was 0.01.
[c] Data cutoff 24 July 2024
[d] 12.3% and 24.0% of patients in the datopotamab deruxtecan and ICC arms, respectively, received subsequent treatment with trastuzumab deruxtecan and/or sacituzumab govitecan post discontinuation.
[e] Predefined p-value boundary was 0.0403.
[f] Endpoints were analysed descriptively.

Figure 1: Kaplan-Meier plot of PFS by BICR in TROPION-Breast01 (data cutoff 17 July 2023)



The improvement in PFS by BICR was consistent amongst the prespecified subgroups of patients including by geographic region, prior use of CDK4/6 inhibitor and previous line of therapy.

Figure 2: Kaplan-Meier plot of final OS in TROPION-Breast01 (data cutoff 24 July 2024)



Number at risk												
Datopotamab deruxtecan (N=365)	365	349	331	299	259	227	180	118	49	12	1	0
ICC (N=367	367	335	309	283	249	213	175	123	51	9	1	0

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with Datroway in all subsets of the paediatric population in breast cancer (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

The pharmacokinetics of datopotamab deruxtecan was evaluated in 729 patients.

At the recommended dosage of Datroway, the geometric mean (coefficient of variation [CV]%) C_{max} of datopotamab deruxtecan and DXd were 154 µg/mL (20.3%) and 2.82 ng/mL (58.1%), respectively, and the AUC (area under the plasma concentration versus time curve) of datopotamab deruxtecan and DXd were 671 µg*day/mL (31.4%) and 18.5 ng*day/mL (42.6%) after the first dose in cycle 1, respectively.

Distribution

Steady state volume of distribution of datopotamab deruxtecan is 3.52 L. *In vitro,* across the concentration range of 10 ng/mL to 100 ng/mL, the mean human plasma protein binding of DXd was 96.8 to 98.0%, and the blood-to-plasma concentration ratio of DXd was 0.59-0.62.

Biotransformation

Datopotamab deruxtecan undergoes intracellular cleavage by lysosomal enzymes to release DXd. The humanised TROP2 IgG1 monoclonal antibody is expected to be degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgG. *In vitro* metabolism studies in human liver microsomes indicate that DXd is primarily metabolised by CYP3A4 via oxidative pathways and does not undergo significant metabolism by UGT or other CYP enzymes.

Elimination

Following intravenous administration of datopotamab deruxtecan in patients, the clearance of datopotamab deruxtecan was estimated to be 0.57 L/day. The median elimination half-life ($t_{1/2}$) of datopotamab deruxtecan was 4.82 days and apparent median $t_{1/2}$ of released DXd was approximately

5.50 days. *In vitro*, DXd was a substrate of P-gp, OATP1B1, OATP1B3, MATE2-K, MRP1 and BCRP. DXd excretion was not studied in humans.

In vitro interactions

Effects of Datroway on the pharmacokinetics of other medicinal products

In vitro studies indicate DXd does not inhibit or induce major CYP450 enzymes including CYP1A2, 2B6, 2C8, 2C9, 2C19, 2D6 and 3A. *In vitro* studies indicate that DXd does not inhibit OAT1, OAT3, OCT1, OCT2, OATP1B1, OATP1B3, MATE1, MATE2-K, P-gp, BCRP or BSEP transporters.

Effects of other medicinal products on the pharmacokinetics of Datroway

In vitro, DXd was a substrate of P-gp, OATP1B1, OATP1B3, MATE2-K, MRP1 and BCRP. No clinically meaningful interaction is expected with medicinal products that are inhibitors of MATE2-K, MRP1, P-gp, OATP1B1 or BCRP transporters (see section 4.5).

Linearity/non-linearity

The exposure of datopotamab deruxtecan and released DXd when administered intravenously increased in proportion to dose in the 4 mg/kg to 10 mg/kg dose range (approximately 0.7 to 1.7 times the recommended dose). No accumulation of datopotamab deruxtecan was observed at the 6 mg/kg dose between cycle 1 and cycle 3.

Special populations

Based on population pharmacokinetic analysis, age (26 to 86 years), race, region, and sex did not have a clinically meaningful effect on exposure of datopotamab deruxtecan or DXd. The mean volume of distribution and clearance of datopotamab deruxtecan and DXd increase with increasing body weight (35.6 kg to 156 kg). This is considered clinically relevant. See section 4.2 for dose recommendations.

Renal impairment

No dedicated renal impairment study was conducted. Based on population pharmacokinetic analysis including patients with mild to moderate (CLcr ≥ 30 and <90 mL/min) renal impairment (estimated by Cockcroft-Gault), the pharmacokinetics of datopotamab deruxtecan or DXd was not affected by mild to moderate renal impairment as compared to normal renal function (CLcr ≥ 90 mL/min) (see section 4.2).

Hepatic impairment

No dedicated hepatic impairment study was conducted. Based on population pharmacokinetic analysis including patients with mild hepatic impairment (total bilirubin ≤ ULN and any AST > ULN or total bilirubin > 1 to 1.5 times ULN and any AST), the pharmacokinetics of datopotamab deruxtecan or DXd was not affected by mild hepatic impairment as compared to normal hepatic function. There are limited data in patients with moderate (total bilirubin > 1.5 to 3 times ULN and any AST) hepatic impairment to draw conclusions. Insufficient data are available for patients with severe (total bilirubin > 3 times ULN and any AST) hepatic impairment. Therefore, patients with moderate and severe hepatic impairment should be monitored carefully (see section 4.2 and 4.4).

5.3 Preclinical safety data

Repeat-dose toxicity

In animals, toxicities were observed in lymphatic and haematopoietic organs, intestines, kidneys, male and female reproductive tracts, lung, skin, eye (cornea), liver and incisor teeth following the administration of datopotamab deruxtecan at exposure levels of the topoisomerase I inhibitor below

clinical plasma exposure. In these animals, ADC exposure levels were similar or above clinical plasma exposure.

Genotoxicity

DXd was clastogenic in both an *in vivo* rat bone marrow micronucleus assay and an *in vitro* Chinese hamster lung chromosome aberration assay.

Carcinogenicity

Carcinogenicity studies have not been conducted with datopotamab deruxtecan.

Reproductive and developmental toxicity

Dedicated fertility studies have not been conducted with datopotamab deruxtecan. Based on the results from an animal toxicity study in rats, datopotamab deruxtecan at 200 mg/kg (approximately 29 times the human recommended dose of 6 mg/kg based on AUC) may impair male and female reproductive function and fertility at exposure levels of the topoisomerase I inhibitor below clinical plasma exposure. Toxicity to male reproductive tract included testis (degeneration of germinal epithelium and atrophy of seminiferous tubule) and epididymis (single cell necrosis of ductal epithelium, cell debris in duct and decreased number of spermatozoa in duct), which did not reverse after 8 weeks of treatment cessation, except for single cell necrosis of ductal epithelium. The effects on female fertility, including an increase in the number of atretic follicles in the ovaries and single cell necrosis of mucosal epithelium in the vagina, may be reversible.

Reproductive and developmental toxicity studies have not been conducted with datopotamab deruxtecan. Based on results from general animal toxicity studies, datopotamab deruxtecan and DXd were toxic to rapidly dividing cells (testes), and DXd was genotoxic, suggesting the potential for embryotoxicity and teratogenicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

L-histidine
L-histidine hydrochloride monohydrate
Sucrose
Polysorbate 80 (E 433)

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

Sodium chloride solution for infusion must not be used for reconstitution or dilution since it may cause particulate formation.

6.3 Shelf life

Unopened vial

4 years.

Reconstituted solution

Chemical and physical in-use stability has been demonstrated for up to 48 hours at 2 °C to 8 °C. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 °C to 8 °C, unless reconstitution has taken place in controlled and validated aseptic conditions.

Diluted solution

It is recommended that the diluted solution be used immediately. If not used immediately, the diluted solution may be stored at room temperature (≤ 25 °C) for up to 4 hours or in a refrigerator at 2 °C to 8 °C for up to 24 hours, including preparation and infusion, protected from light.

6.4 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C).
Do not freeze.

For storage conditions after reconstitution and dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Datroway is provided in a 10 mL Type 1 amber borosilicate glass vial sealed with a fluoro-resin laminated butyl rubber stopper, and a polypropylene/aluminium blue flip-off crimp cap.

Each carton contains 1 vial.

6.6 Special precautions for disposal and other handling

Datroway contains a cytotoxic component and should be administered under the supervision of a physician experienced in the use of cytotoxic agents. Appropriate procedures for proper preparation, handling and disposal of antineoplastic and cytotoxic medicinal products should be used.

Appropriate aseptic technique should be used for the following reconstitution and dilution procedures.

Reconstitution

- Reconstitute immediately before dilution.
- More than one vial may be needed for a full dose. Calculate the dose (mg), the total volume of reconstituted Datroway solution required, and the number of vial(s) of Datroway needed (see section 4.2).
- Reconstitute each 100 mg vial using a sterile syringe to slowly inject 5 mL of water for injection into each vial to obtain a final concentration of 20 mg/mL.
- Swirl the vial gently until completely dissolved. Do not shake.
- From a microbiological point of view, the product should be used immediately. If not used immediately, chemical and physical in-use stability has been demonstrated for up to 48 hours at 2 ºC to 8 ºC. Store the reconstituted Datroway vials in a refrigerator at 2 °C to 8 °C, protected from light. Do not freeze.
- The reconstituted product contains no preservative and is intended for single use only.

Dilution

- Withdraw the calculated amount from the vial(s) using a sterile syringe. Inspect the reconstituted solution for particulates and discolouration. The solution should be clear and colourless to light yellow. Do not use if visible particles are observed or if the solution is cloudy or discoloured.

- Dilute the calculated volume of reconstituted Datroway in an infusion bag containing 100 mL of 5% glucose solution. Do not use sodium chloride solution (see section 6.2). An infusion bag made of polyvinylchloride (PVC) or polyolefin (polypropylene (PP) or copolymer of ethylene and propylene) is recommended.
- Gently invert the infusion bag to thoroughly mix the solution. Do not shake.
- Cover the infusion bag to protect from light.
- If not used immediately, store at room temperature (≤ 25 °C) for up to 4 hours including preparation and infusion, or in a refrigerator at 2 °C to 8 °C for up to 24 hours, protected from light. Do not freeze.
- Discard any unused portion left in the vial.

Administration

- If the prepared infusion solution was stored refrigerated (2 °C to 8 °C), it is recommended that the solution be allowed to reach to room temperature prior to administration, protected from light.
- Administer Datroway as an intravenous infusion only with an infusion line and tubing set made of PVC, polybutadiene (PBD), or low density polyethylene (LDPE).
- Administer Datroway with a 0.2 micron in-line polytetrafluoroethylene (PTFE), polyethersulfone (PES) or nylon 66 filter.
- Do not administer as an intravenous push or bolus (see section 4.2).
- Cover the infusion bag to protect from light.
- Do not mix Datroway with other medicinal products or administer other medicinal products through the same intravenous line.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Daiichi Sankyo Europe GmbH
Zielstattstrasse 48
81379 Munich
Germany

8. MARKETING AUTHORISATION NUMBER

EU/1/25/1915/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 04 April 2025

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

ANNEX II

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers of the biological active substance

Daiichi Sankyo Co. Ltd.
Onahama Plant
389-4 Aza Otsurugi, Izumimachi Shimogawa, Iwaki
Fukushima 971-8183
Japan

Lonza AG
Lonzastrasse
3930 Visp
Switzerland

Name and address of the manufacturer responsible for batch release

Daiichi Sankyo Europe GmbH
Luitpoldstrasse 1
85276 Pfaffenhofen
Germany

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription. (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or

as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Datroway 100 mg powder for concentrate for solution for infusion
datopotamab deruxtecan

2. STATEMENT OF ACTIVE SUBSTANCE

One vial of powder for concentrate for solution for infusion contains 100 mg of datopotamab deruxtecan.
After reconstitution, one vial of 5 mL solution contains 20 mg/mL of datopotamab deruxtecan.

3. LIST OF EXCIPIENTS

Excipients: L-histidine, L-histidine hydrochloride monohydrate, sucrose, polysorbate 80 (E 433).
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for concentrate for solution for infusion
1 vial

5. METHOD AND ROUTE OF ADMINISTRATION

for intravenous use after reconstitution and dilution

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING, IF NECESSARY

cytotoxic

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Daiichi Sankyo Europe GmbH
81366 Munich
Germany

12. MARKETING AUTHORISATION NUMBER

EU/1/25/1915/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Datroway 100 mg powder for concentrate
datopotamab deruxtecan
for IV use after reconstitution and dilution

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

100 mg

6. OTHER

cytotoxic

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Datroway 100 mg powder for concentrate for solution for infusion
datopotamab deruxtecan

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your healthcare provider (doctor, pharmacist or nurse).
- If you get any side effects, talk to your healthcare provider. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Datroway is and what it is used for

Datroway is a medicine that contains the active substance datopotamab deruxtecan.

Datroway is used to treat adults who have been diagnosed with a type of cancer known as hormone receptor positive (HR+) and human epidermal growth factor receptor 2 (HER2)-negative breast cancer. It is used when the cancer has spread to other parts of the body or cannot be removed by surgery in patients who have received hormone therapy and at least one additional cancer treatment for unresectable or metastatic disease.

One part of the medicine is a monoclonal antibody (datopotamab) that attaches specifically to cells that have the protein TROP2, which is present in larger numbers on the surface of TROP2-expressing breast cancer cells. The other active part of Datroway is DXd, a substance that can kill cancer cells. Once the medicine has attached to TROP2-expressing cancer cells, the DXd enters the cells and kills them.

2. What you need to know before you are given Datroway

You must not be given Datroway

- if you are allergic to datopotamab deruxtecan or any of the other ingredients of this medicine (listed in section 6).

If you are not sure if you are allergic, talk to your doctor or nurse before you are given Datroway.

Warnings and precautions

Talk to your doctor or nurse before you are given Datroway, or during treatment if you have:
- cough, shortness of breath, fever, or other new or worsening breathing problems. These may be symptoms of a serious and potentially fatal lung disease called interstitial lung disease. A

history of lung disease may increase the risk of developing interstitial lung disease. Your doctor may have to monitor your lungs while you are taking this medicine.

Datroway may also cause:

- eye problems. You should use preservative-free lubricating eye drops several times daily to prevent dry eye and other eye problems. You should avoid the use of contact lenses during treatment. If you have or develop eye problems, which may include dry eyes, increased tears, sensitivity to light or vision changes during treatment, contact your doctor or nurse. Your doctor may refer you to an eye care provider if needed.
- mouth ulcers and sores. In addition to good oral hygiene and dietary recommendations, your doctor or nurse will also recommend a non-alcoholic mouthwash to use 4 times a day. This mouthwash may contain steroids. If you develop pain, discomfort, or open sores in your mouth, tell your doctor or nurse. Follow your doctor or nurse's instructions on how to use mouthwash to prevent or treat mouth ulcers and sores.

If you have liver problems; your doctor may have to monitor you more closely while you are taking this medicine.

Children and adolescents

Datroway is not recommended for anyone under the age of 18 years: there is no information on how well it works in this age group.

Other medicines and Datroway

Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines.

Contraception

You should use effective contraception (birth control) to avoid becoming pregnant while being treated with Datroway and for a period of time after your last dose.

- Women taking Datroway should continue contraception for at least 7 months after the last dose of Datroway.

- Men taking Datroway whose partner may become pregnant should continue using effective contraception for at least 4 months after the last dose of Datroway.

Talk to your doctor about the best contraception for you. Also talk to your doctor before you stop your contraception.

Pregnancy

Datroway is **not recommended** during pregnancy because this medicine may harm the unborn baby. Speak with your doctor immediately if you are pregnant, think you may be pregnant or are planning to become pregnant before or during treatment.

Breast-feeding

You should not breast-feed during treatment with Datroway and for at least 1 month after your last dose. This is because it is not known whether Datroway passes into breast milk. Talk to your doctor about this.

Fertility

If you are being treated with Datroway, you should take advice on conserving sperm or eggs (ova) before treatment because the medicine may reduce your fertility. Therefore, discuss this with your

doctor before starting treatment.

Driving and using machines

Datroway could impact your ability to drive or use machines. Be careful if you feel tired or have trouble seeing.

Datroway contains polysorbate 80

This medicine contains 1.5 mg of polysorbate 80 in each vial. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

3. How you are given Datroway

Datroway will be given to you in a hospital or clinic by a doctor or nurse experienced in the use of cancer medicines.

The recommended dose is 6 mg for every kilogram of your body weight, every 3 weeks. Your doctor or nurse will calculate the dose you need based on your body weight and will decide how many treatments you need.

Your doctor or nurse will give you Datroway as an infusion (drip) into your vein.

Your first infusion will be given over 90 minutes. If this goes well, the infusion on your next visits may be given over 30 minutes.

After each infusion, you will be monitored for side effects for 30 minutes. Your doctor or nurse may lower your dose, or temporarily or permanently stop your treatment depending on your side effects.

Before each Datroway infusion, your doctor or nurse may give you medicines to help prevent nausea, vomiting, and infusion-related reactions.

Before each Datroway infusion and during the treatment period, your doctor or nurse may recommend using a mouthwash to help prevent mouth ulcers and sores. If you get infusion-related symptoms, your doctor or nurse may slow down your infusion or interrupt or stop your treatment.

During the treatment period, you should use preservative-free lubricating eye drops several times daily and avoid the use of contact lenses.

If you miss an appointment to get Datroway

Contact your doctor or treatment centre right away to reschedule your appointment.
It is very important that you do not miss a dose of this medicine.

If you stop receiving Datroway

Do not stop treatment with Datroway without checking with your doctor or nurse.
If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Tell your doctor or nurse if you get any side effects, including those not listed in this leaflet.

Some side effects may be serious, and possibly fatal. **Speak with your doctor or nurse immediately** if you notice any of the following:

Very common (may affect more than 1 in 10 people):
- Mouth ulcers and sores (stomatitis).
- Inflammation of the cornea (keratitis). Symptoms can include dry eyes, increased tears, sensitivity to light or vision changes. Inflammation of the cornea (the transparent layer in front of the eye that covers the pupil and iris) may lead to an ulcer.

Common (may affect up to 1 in 10 people):
- Interstitial lung disease. Symptoms can include cough, shortness of breath, fever, or other new or worsening breathing problems.

Getting medical treatment right away may help keep these problems from becoming more serious.

Other side effects

The frequency and severity of side effects may vary with the dose you received. Tell your doctor or nurse if you notice any of the following side effects:

Very common (may affect more than 1 in 10 people)
- nausea (feeling sick)
- tiredness (fatigue)
- hair loss (alopecia)
- constipation
- vomiting
- dry eye
- COVID-19
- low levels of red blood cells (anaemia), as seen in blood tests
- decreased appetite
- increased levels of liver enzyme (aspartate aminotransferase) in the blood
- rash
- diarrhoea
- low levels of neutrophils, a type of white blood cell that fights infection (neutropenia)
- increased levels of liver enzyme (alanine aminotransferase) in the blood

Common (may affect up to 1 in 10 people)
- redness and discomfort in the eye (conjunctivitis)
- infusion-related reactions. These may include fever, chills, itching or rash
- increased tears production
- infection of the parts of the body that collect and pass out urine
- dry skin
- dry mouth
- itching (pruritus)
- inflammation of the eyelid (blepharitis)
- difficulty breathing (dyspnoea)
- taste disturbance (dysgeusia)
- dysfunction of the glands of the eyelids (meibomian glands)
- skin discoloration (hyperpigmentation)
- blurred vision
- infection of the lungs
- low levels of white blood cells which fight infection (leukopenia)
- loss of eyelashes (madarosis)
- abnormal sensitivity of the eyes to light

- shiver, fever, general discomfort, pale or discoloured skin, shortness of breath due to overwhelmed bloodstream by bacteria (sepsis)

Uncommon (may affect up to 1 in 100 people)
- visual impairment

Reporting of side effects

If you get any side effects, talk to your healthcare provider. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Datroway

Datroway will be stored by healthcare professionals at the hospital or clinic where you receive treatment. The following information is intended for your doctor or nurse.

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the outer carton and vial after EXP. The expiry date refers to the last day of that month.
- Store in a refrigerator (2 °C – 8 °C). Do not freeze.
- The prepared solution for infusion is stable for up to 24 hours at 2 °C – 8 °C protected from light and must be discarded thereafter.

Applicable special handling and disposal procedures must be followed. Your healthcare provider is responsible for disposing of any unused Datroway correctly. These measures will help protect the environment.

6. Contents of the pack and other information

What Datroway contains

- The active substance is datopotamab deruxtecan.
  One vial of powder for concentrate for solution for infusion contains 100 mg of datopotamab deruxtecan. After reconstitution, one vial of 5 mL solution contains 20 mg/mL of datopotamab deruxtecan.
- The other ingredients are L-histidine, L-histidine hydrochloride monohydrate, sucrose and polysorbate 80 (see section 2).

What Datroway looks like and contents of the pack

Datroway is a white to yellowish white lyophilised powder supplied in a clear amber vial with a rubber stopper, aluminium seal and plastic flip-off cap.
Each carton contains 1 vial.

Marketing Authorisation Holder
Daiichi Sankyo Europe GmbH
Zielstattstrasse 48
81379 Munich
Germany

Manufacturer
Daiichi Sankyo Europe GmbH
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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

The following information is intended for healthcare professionals only:

Datroway contains a cytotoxic component and should be administered under the supervision of a physician experienced in the use of cytotoxic agents. Appropriate procedures for proper preparation, handling and disposal of antineoplastic and cytotoxic medicinal products should be used.

Appropriate aseptic technique should be used for the following reconstitution and dilution procedures.

Reconstitution
- Reconstitute immediately before dilution.
- More than one vial may be needed for a full dose. Calculate the dose (mg), the total volume of reconstituted Datroway solution required, and the number of vial(s) of Datroway needed.
- Reconstitute each 100 mg vial using a sterile syringe to slowly inject 5 mL of water for injection into each vial to obtain a final concentration of 20 mg/mL.
- Swirl the vial gently until completely dissolved. Do not shake.
- From a microbiological point of view, the product should be used immediately. If not used immediately, chemical and physical in-use stability has been demonstrated for up to 48 hours at 2 ºC to 8 ºC. Store the reconstituted Datroway vials in a refrigerator at 2 °C to 8 °C, protected from light. Do not freeze.
- The reconstituted product contains no preservative and is intended for single use only.

Dilution
- Withdraw the calculated amount from the vial(s) using a sterile syringe. Inspect the reconstituted solution for particulates and discolouration. The solution should be clear and colourless to light yellow. Do not use if visible particles are observed or if the solution is cloudy or discoloured.
- Dilute the calculated volume of reconstituted Datroway in an infusion bag containing 100 mL of 5% glucose solution. Do not use sodium chloride solution. An infusion bag made of polyvinylchloride (PVC) or polyolefin (polypropylene (PP) or copolymer of ethylene and propylene) is recommended.
- Gently invert the infusion bag to thoroughly mix the solution. Do not shake.
- Cover the infusion bag to protect from light.
- If not used immediately, store at room temperature (≤ 25 °C) for up to 4 hours including preparation and infusion, or in a refrigerator at 2 °C to 8 °C for up to 24 hours, protected from light. Do not freeze.
- Discard any unused portion left in the vial.

Administration

- If the prepared infusion solution was stored refrigerated (2 °C to 8 °C), it is recommended that the solution be allowed to reach to room temperature prior to administration, protected from light.
- Administer Datroway as an intravenous infusion only with an infusion line and tubing set made of PVC, polybutadiene (PBD), or low density polyethylene (LDPE).
- Administer Datroway with a 0.2 micron in-line polytetrafluoroethylene (PTFE), polyethersulfone (PES) or nylon 66 filter.
- Do not administer as an intravenous push or bolus.
- Cover the infusion bag to protect from light.
- Do not mix Datroway with other medicinal products or administer other medicinal products through the same intravenous line.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.